

**Amendments to the Claims**

Please amend claim 1-3, 6, 10, and 12, as set forth below. Please cancel claims 15-18. Please add new claims 76-78.

The current listing of claims replaces all prior listings.

1. (Currently amended) A method of identifying an agent that ~~[modulates]~~ indirectly inhibits reverse transcriptase ~~[activity in a cell,]~~ by elevating the intracellular manganese ion concentration in a cell comprising:  
    contacting [a] ~~the~~ cell ~~[membrane comprising a divalent cation-transporting protein, which transports manganese ions,]~~ with a test agent; and  
    detecting ~~[altered]~~ elevated intracellular manganese ion levels in the cell [manganese ion transport due to] after contact with the test agent as compared to manganese ion [transport] levels in the absence of the test agent, wherein ~~[detecting altered manganese ion transport comprises detecting altered reverse transcriptase activity, which activity is separate from the contacted cell membrane, thereby identifying]~~ a test agent that results in elevations of intracellular manganese ion levels is indicative of an agent that ~~[modulates]~~ inhibits reverse transcriptase activity in a cell.
2. (Currently Amended) The method of claim 1, wherein the cell~~[ular membrane]~~ comprises an isolated cell membrane.
3. (Currently Amended) The method of claim [1] 2, wherein the cell membrane comprises a eukaryotic cell membrane.
4. (Original) The method of claim 3, wherein the eukaryotic cell membrane comprises a yeast cell membrane or a mammalian cell membrane.
5. (Original) The method of claim 3, wherein the eukaryotic cell membrane comprises a human cell membrane.

6. (Currently Amended) The method of claim 1, wherein contacting the cell ~~[membrane]~~ comprises contacting a cell comprising the cell membrane.

7. (Original) The method of claim 6, wherein the cell comprises a yeast cell.

8. (Original) The method of claim 6, wherein the cell comprises a human cell.

9. (Original) The method of 6, wherein the cell comprises a T lymphocyte.

10. (Currently Amended) The method of claim 1, wherein the cell comprises a divalent cation transport protein compris[es]ing a P-type ATPase.

11. (Original) The method of claim 10, wherein the ATPase is a Pmr1p protein or a homolog thereof.

12. (Currently Amended) The method of claim 1, wherein the test agent does not alter transport of a divalent cation other than manganese ions by [the] a divalent cation transporting protein.

13. (Original) The method of claim 1, wherein the agent reduces or inhibits manganese ion transport out of a cell.

14. (Original) The method of claim 1, wherein the agent reduces or inhibits manganese ion transport into a cell.

15. (Canceled)

16. (Canceled)

17. (Canceled)

18. (Canceled)

19. (Previously presented) The method of claim 1, wherein reverse transcriptase activity is measured using a polyribonucleotide template.

20. (Previously presented) The method of claim 1, wherein reverse transcriptase activity is measured using a polydeoxyribonucleotide template.

21. (Withdrawn) An agent identified according to the method of claim 1, wherein the agent modulates reverse transcriptase activity in a cell.

22. (Withdrawn) A method of identifying an agent that modulates reverse transcriptase activity in a cell, comprising:  
contacting a cell expressing a reverse transcriptase with a test agent; and  
detecting altered reverse transcriptase activity due to contact with the test agent as compared to reverse transcriptase activity in the absence of the test agent, wherein the test agent alters manganese ion concentration in the cell, thereby identifying an agent that modulates reverse transcriptase activity in a cell.

23. (Withdrawn) The method of claim 22, wherein detecting reverse transcriptase activity comprises measuring cDNA produced by the reverse transcriptase using a polynucleotide template in the cell.

24. (Withdrawn) The method of claim 23, wherein the polynucleotide template comprises a retrotransposable element.

25. (Withdrawn) The method of claim 24, wherein the retrotransposable element comprises a transposon.

26. (Withdrawn) The method of claim 25, wherein the transposon comprises a Ty transposon.

27. (Withdrawn) The method of claim 26, wherein the Ty transposon comprises a Ty-1 transposon.

28. (Withdrawn) The method of claim 24, wherein the retrotransposable element comprises a retrovirus.

29. (Withdrawn) The method of claim 22, wherein the reverse transcriptase comprises a retrovirus reverse transcriptase.

30. (Withdrawn) The method of claim 29, wherein the retrovirus reverse transcriptase comprises a human immunodeficiency virus reverse transcriptase or an avian myeloblastosis virus reverse transcriptase.

31. (Withdrawn) The method of claim 22, wherein the cell comprises a yeast cell, an avian cell, or a mammalian cell.

32. (Withdrawn) The method of claim 22, wherein the cell comprises a *Saccharomyces cerevisiae* cell.

33. (Withdrawn) The method of claim 22, wherein the cell comprises a human cell.

34. (Withdrawn) The method of claim 22, which is performed in a high throughput format, wherein the cell comprises one of a plurality of cells.

35. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is the same or different, or a combination thereof.

36. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is arranged in an array.

37. (Withdrawn) The method of claim 36, wherein the array is an addressable array.

38. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is on a microchip, on a glass slide, on a bead, or in a well.

39. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is contacted with a test agent, which is the same or different or a combination thereof.

40. (Withdrawn) The method of claim 34, wherein the cell is a yeast cell, said plurality of cells comprising a plurality of yeast cells.

41. (Withdrawn) The method of claim 40, wherein the yeast cell expresses a human divalent cation transporting protein.

42. (Withdrawn) The method of claim 41, wherein the human divalent cation transporting protein comprises a human Pnmp1 transporting protein.

43. (Withdrawn) The method of claim 22, wherein the cell comprises a sample obtained from a subject.

44. (Withdrawn) An agent identified according to the method of claim 22, wherein the agent modulates reverse transcriptase activity in a cell.

45. (Withdrawn) A method of modulating reverse transcriptase activity in a cell, comprising contacting the cell with an agent that alters manganese ion transport across a cell membrane of the cell, thereby modulating reverse transcriptase activity in the cell.

46. (Withdrawn) The method of claim 45, wherein the agent reduces or inhibits manganese ion transport out of the cell.

47. (Withdrawn) The method of claim 45, wherein the agent that alters manganese ion transport does not alter transport of a divalent cation other than manganese ion.

48. (Withdrawn) The method of claim 45, wherein the agent alters the activity of a divalent cation transporting protein in a cell membrane of the cell.

49. (Withdrawn) The method of claim 48, wherein the divalent cation transporting protein comprises a P-type ATPase.

50. (Withdrawn) The method of claim 49, wherein the P-type ATPase comprises a Pmr1p protein or a homolog thereof.

51. (Withdrawn) A method of modulating reverse transcriptase activity, comprising contacting a reverse transcriptase with a predetermined concentration of manganese ions, thereby modulating reverse transcriptase activity.

52. (Withdrawn) The method of claim 51, further comprising contacting the reverse transcriptase with a predetermined concentration of magnesium ions.

53. (Withdrawn) The method of claim 51, wherein modulating the reverse transcriptase activity comprises increasing relative reverse transcriptase activity for a polyribonucleotide template as compared to a polydeoxyribonucleotide template.

54. (Withdrawn) The method of claim 51, wherein the reverse transcriptase is a human immunodeficiency virus reverse transcriptase.

55. (Withdrawn) A method of ameliorating a retrovirus infection in a subject, comprising administering an agent that alters manganese ion transport in a retrovirus infected cell of the subject, thereby ameliorating the retrovirus infection.

56. (Withdrawn) The method of claim 55, wherein the agent reduces or inhibits a divalent cation transporting protein activity in the retrovirus infected cell.

57. (Withdrawn) The method of 56, wherein the agent does not alter transport of a divalent cation other than a manganese ion by the divalent cation transporting protein.

58. (Withdrawn) The method of claim 56, wherein the divalent cation transporting protein comprises a Pmr1p protein or a homologue thereof.

59. (Withdrawn) The method of claim 55, wherein the subject is a human subject.

60. (Withdrawn) The method of claim 55, wherein the retrovirus infected cell comprises a human T lymphocyte.

61. (Withdrawn) A high throughput assay for identifying an agent that alters manganese ion transport by a divalent cation transporting protein in a cell, comprising an array comprising a plurality of cells that express a heterologous divalent cation transporting protein, wherein the heterologous divalent cation transporting protein transports at least manganese ion.

62. (Withdrawn) The high throughput assay of claim 61, wherein the plurality of cells comprises a plurality of yeast cells.

63. (Withdrawn) The high throughput assay of claim 62, wherein the heterologous divalent cation transporting protein comprises a human divalent cation transporting protein.

64. (Withdrawn) The high throughput assay of claim 63, wherein the human divalent cation transporting protein comprises a human Pmrp1 transporting protein.

65. (Withdrawn) The high throughput assay of claim 61, wherein the array comprises an array of wells, wherein cells of the plurality are contained in the wells.

66. (Withdrawn) The high throughput assay of claim 61, wherein cells of the plurality of cells further express a reporter gene.

67. (Withdrawn) The high throughput assay of claim 66, wherein expression of the reporter gene in a cell of the plurality is regulated by manganese ion concentration in the cell.

68. (Withdrawn) The high throughput assay of claim 66, wherein expression of the reporter gene in a cell of the plurality is regulated by reverse transcriptase activity in the cell.

69. (Withdrawn) A method of identifying an agent that modulates reverse transcriptase activity in a cell, comprising:

contacting cells of an array of cells with at least one test agent, wherein the cells comprise a divalent cation transporting protein, which transports manganese ions; and  
detecting altered manganese ion transport in cells of the array due to contact with the test agent as compared to manganese ion transport in the absence of the test agent, thereby identifying an agent that modulates reverse transcriptase activity in a cell.



70. (Withdrawn) The method of claim 69, wherein cells of the array are eukaryotic cells.
71. (Withdrawn) The method of claim 70, wherein the eukaryotic cells are yeast cells or mammalian cells.
72. (Withdrawn) The method of claim 69, wherein the divalent cation transporting protein expressed by the cells of the array is a heterologous divalent cation transporting protein transports.
73. (Withdrawn) The method of claim 72, wherein the cells of the array comprise yeast cells.
74. (Withdrawn) The method of claim 72, wherein the heterologous divalent cation transporting protein comprises a human divalent cation transporting protein.
75. (Withdrawn) The method of claim 74, wherein the human divalent cation transporting protein comprises a human Pmp1 transporting protein.
76. (New) A method of identifying an agent that inhibits reverse transcriptase indirectly by elevating intracellular manganese ion concentration comprising:  
    contacting a cell membrane with a test agent; and  
    detecting elevated manganese ion levels in the cell after contact with the test agent as compared to manganese ion levels in the absence of the test agent, wherein a test agent that results in elevations of manganese ion levels is indicative of an agent that inhibits reverse transcriptase activity in a cell.
77. (New) The method of claim 1, wherein the agent increases manganese ion transport into a cell.

78. (New) The method of claim 1, wherein the cell comprises a divalent cation transport protein comprising an ATPase.